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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/562,615	07/27/2006	Myung-Hwa Kim	428.1145	6138

20311 7590 05/10/2011

LUCAS & MERCANTI, LLP
475 PARK AVENUE SOUTH
15TH FLOOR
NEW YORK, NY 10016

EXAMINER	
SZNAIDMAN, MARCOS L	
ART UNIT	PAPER NUMBER
1628	

NOTIFICATION DATE	DELIVERY MODE
05/10/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

info@lmiplaw.com

Office Action Summary	Application No.	Applicant(s)	
	10/562,615	KIM ET AL.	
	Examiner	Art Unit	
	MARCOS L. SZNAIDMAN	1628	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 April 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *12,13 and 16-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12,13 and 16-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This office action is in response to applicant's reply filed on April 4, 2011.

Status of Claims

Amendment of claims 12, 16-17 is acknowledged.

Claims 12-13 and 16-21 are currently pending and are the subject of this office action.

Claims 12-13 and 16-21 are presently under examination.

The examination was expanded in a prior office action dated 06/29/10 to the entire genus encompassed by Formula I.

Priority

The present application is a 371 of PCT/KR04/01518 filed on 06/23/2004, and claims priority to foreign Application: REPUBLIC OF KOREA 10-2003-00415467 filed on 06/25/2003.

Rejections and/or Objections and Response to Arguments

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated (Maintained Rejections and/or Objections) or newly applied (New Rejections and/or Objections, Necessitated by Amendment or New Rejections and/or Objections not

Necessitated by Amendment). They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 103 (Maintained Rejection)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

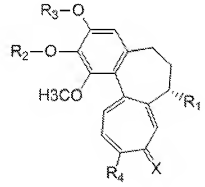
The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

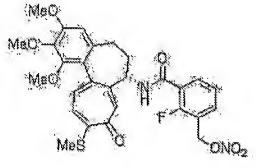
Claims 12-13 and 16-21 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Kim et. al. (WO 02/100824, cited in prior office action) in view of Patani et. al. (Chem. Rev. (1996) 96:3147-3176, cited in prior office action).

Claims 12-13 and 16-17 recite a tricyclic derivative represented by the following Formula I or pharmaceutically acceptable salts thereof:

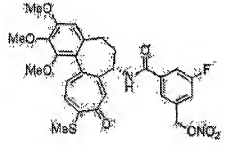


Formula I

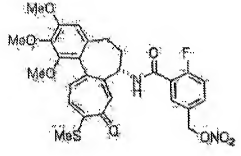
More specifically claim 17 recites the following compounds:



Compound 10

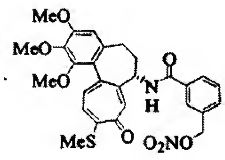


Compound 12



Compound 17

For claims 12-13 and 16-21, Kim teaches the following compound:



(see example 12 on page 28, from now on compound A)

Kim does not teach the above instant compounds: 10, 12, and 17. However, compound A differs from the instant compounds in the presence of a Hydrogen atom instead of Fluorine atom in the aromatic ring. Patani teaches that the substitution of Hydrogen by Fluorine is one of the most commonly employed monovalent isosteric replacements (see page 3149, left column under 1. Fluorine vs. Hydrogen Replacements). Further in Figure 2 on the same page they give an example wherein replacing Hydrogen with Fluorine in an aromatic ring maintains or improves the pharmacological properties of the compounds. In summary, substituting Hydrogen by Fluorine is routine practice in the pharmaceutical art, and should have similar biological/pharmaceutical properties.

Further, MPEP 2144, Section III states: prior art structures do not have to be true homologs or isomers to render structurally similar compounds *prima facie* obvious. *In re Payne*, 606 F.2d 303, 203 USPQ 245 (CCPA 1979) (Claimed and prior art compounds were both directed to heterocyclic carbamoyloximino compounds having pesticidal activity. The only structural difference between the claimed and prior art was

that the ring structures of the claimed compounds had two carbon atoms between two sulfur atoms, whereas the prior art ring structures had either one or three carbon atoms between two sulfur atoms. The court held that although the prior art compounds were not true homologs or isomers of the claimed compounds, the similarity between the chemical structures and properties is sufficiently close that one of ordinary skill in the art would have been motivated to make the claimed compounds in searching for new pesticides). In *re Gyurik*, 201 USPQ 552, 596 F2d 1012 on page 557 states: "In obviousness rejections based on close similarity in chemical structure, the necessary motivation to make a claimed compound, and thus the *prima facie* case of obviousness, rises from the expectation that compounds similar in structure will have similar properties." In this case it is expected, as discussed above (see Patani's reference), that compounds differing only by the presence or absence of Fluorine in the aromatic ring would have similar chemical, physical and biochemical properties.

At the time of the invention, it would have been *prima facie* obvious for a person of ordinary skill in the art to replace any Hydrogen of the aromatic ring of compound A with a Fluorine in order to obtain either compound: 10, 12, or 17, and expect these compounds to have the similar biological/pharmaceutical properties, since the prior art teaches replacing Hydrogen with Fluorine is routine practice in the pharmaceutical art, in order to obtain molecules with similar or better pharmaceutical properties, thus resulting in the practice of claims 12-13 and 16-17 with a reasonable expectation of success.

For claims 18-21, Kim further teaches that the compounds of the invention can be used as pharmaceutical compositions that are effective as anticancer, antiproliferation and immunosuppressive agents (see technical field on page 1). The pharmaceutical composition contains common excipients (see page 19).

At the time of the invention, it would have been *prima facie* obvious for a person of ordinary skill in the art to further make a pharmaceutical composition of the above compounds using common excipients as suggested by Kim, in order to obtain a better way of administering the drug, thus resulting in the practice of claims 18-21 with a reasonable expectation of success.

Response to Applicant's arguments related to the above rejection

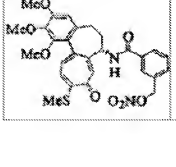
Applicant's arguments have been fully considered but are not persuasive.

Applicant argues that:

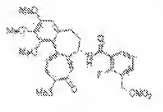
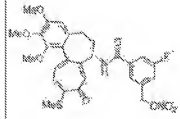
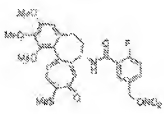
-Fluorinated compound with superior anticancer activity-

First of all, the present invention provides the anticancer activities of the inventive compounds including compounds 10, 12, and 17, which are fluorinated on various positions on Compound A. KIM and the present invention both measured their anti-cancer efficacy of the compound against several cancer cell lines using a known anti-cancer agent, paclitaxel, as the control. Table 1 and 2 provides analysis of their activities against paclitaxel. It is noted that there are three common cancer cell lines these compounds were tested against, A549, SK-OV-3 and MCF-7. The compounds of the present invention shows equal or significant improvement in several cell lines compared to Compound A. The data marked as "*" shows that the compounds in the present invention can be 2-15 times more effective than Compound A. Especially for MCF-7 cell line, Compounds 10, 12 and 17 of the instant invention shows predominantly superior efficacy than Compound A.

[Table 1] Cytotoxicity to cancer cell lines for compound 12 (Compound A) of Kim et al., data from Table

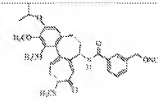
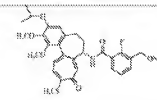
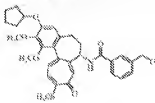
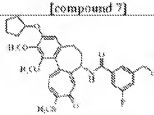
	Cytotoxicity [ED_{50} nM]				
Cell line	A549	SK-OV-3	SK-MEL-2	HCT15	MCF-7
Taxol	0.3	1.2	0.1	0.1	0.04
Example 12	0.1	0.3	0.1	0.1	0.2
(Compound A) 	3 times	4 times	1 times	1 times	0.2 times

[Table 2] Cytotoxicity to cancer cell lines for compounds 10, 12 and 17 of present invention, data from Table 1 on pages 139-140 of the present application.

	Cytotoxicity [ED_{50}, nM]				
Cell line	A549	SK-OV-3	SK-MEL-2	HCT15	MCF-7
Paclitaxel	0.3	1.2	0.1	0.1	0.9
Cpd. 10 	0.28 1 times	0.23 4 times	0.12 1 times	0.39 0.25 times	0.09 10 TIMES*
Cpd. 12 	0.05 6 TIMES*	0.27 4 times	0.11 1 times	0.05 2 TIMES*A	0.03 30 TIMES*
Cpd. 17 	0.21 1.5 times	0.19 6 TIMES*	0.17 1 times	0.19 0.5 times	0.08 11 TIMES*

A similar effect of fluoride on the biological activity can be also found among the compounds in the present application. Compounds 9 and 15 are fluorinated counterpart of compounds 3 and 7, respectively.

[Table 3] Compounds in the present application with H vs. F

	Cytotoxicity [ED_{50}: nM]				
Cell lines	A549	SK-OV-3	SK-MEL-2	HCT15	MCF-7
 [compound 3]	2.4	4.0	1.0	4.8	2.3
 [compound 9]	0.49	0.84	0.22	0.64	0.13
 [compound 7]	>50	>50	>50	>50	>50
 [compound 15]	36.2	>50	22.5	23.4	18.6

Examiner's response:

First:

In *re Gyurik*, 201 USPQ 552, 596 F2d 1012 on page 557 states: "In obviousness rejections based on close similarity in chemical structure, the necessary motivation to make a claimed compound, and thus the *prima facie* case of obviousness, rises from the expectation that compounds similar in structure will have similar properties."

In the instant case, the prior art teaches compound A (see above) which only differs from the instant compounds 10, 12, and 17 in the presence of an Hydrogen atom instead of Fluorine in the aromatic ring. According to Patani (see above): "The substitution by Fluorine is one of the more commonly employed monovalent isosteric replacements" (see page 3149, left column, first sentence under 1. Fluorine vs. Hydrogen Replacements). Then Patani shows some examples, in particular Figure 2 and Table 4 (see page 3149, right column) wherein the substitution of an Hydrogen atom of an aromatic ring with a Fluorine atom causes some improvement in the biological properties of these compounds.

Obviously, no one can predict with 100% certainty that replacing an Hydrogen atom with a Fluorine will produce a molecule with less, equal or more activity than the apparent one, or how different the activities will be, however, the point to be made is that based on the teachings of the prior art (see Patani) there is a reasonable expectation that replacing an Hydrogen atom of an aromatic ring of a biologically active molecule will produce another molecule that will have "similar" biological properties to the parent one. By "similar" it is meant less, more or equal.

The data presented by Applicant in Tables 1 and 2 confirms the above prediction: the data for the cell lines: A549, SK-OV-3, SK-MEL-2 and HCT15 are very similar for the fluorinated and non-fluorinated compounds. For the MCF-7 cell line, as Applicant pointed out, the data shows some improvement (10 to 30 times) in the activity of the fluorinated compounds. However, this improvement can not be considered unexpected, since in the case presented by Patani Figure 2 and Table 4 (see page 3149, right column) wherein the substitution of an Hydrogen atom of an aromatic ring with Fluorine causes some improvement (4 (1000/260) to 18 times (1000/5)) in their biological properties. So the magnitude of the variation in the potency (10 to 30 times) obtained by replacing Hydrogen with Fluorine in the instant compounds is not unexpected or unusual.

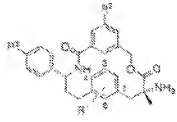
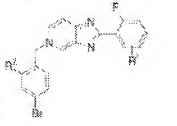
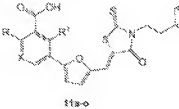
Table 3 further emphasizes the concept that within certain range compounds differing only in the presence or absence of a Fluorine atom in an aromatic ring will have similar biological properties (some will fare better, some will fare worse). For example compound 9, which is the Fluorinated counterparts of compound 3, shows better 4 to 17 times) cytotoxic properties in all cell lines, which confirms what was mentioned above, that within certain range the fluorinated compounds will have "similar" properties than their non-fluorinated counterparts.

Applicant argues that:

-Fluorinated compounds with reduced biological activity-

On the other hand, substitution of fluorinated is not always obviously expected to improve the biological activity of the compounds. Some experimental report known to those skilled in the art can also teach away or discourage those ordinary skilled in the art from making fluorinated compounds randomly. Applicant respectfully provides the following data from non-patent literature wherein fluorination reduced the biological activity of a compound. In the following publications, many fluorinated compounds have reduced biological activities compared to their non-fluorinated counterpart.

[Table 4] Compounds in the literature wherein F reduces activity

Compound	Result
Exhibit_BMCL_4057 	This publication reports Structure-Activity Relation (SAR) of BACE-1 inhibitors. The result in Table 2 shows that the fluorinated Compound 6c (R^1=F, R^2=2-CN-Ph, R^3=F) has a much lower activity than non-fluorinated compound 6b (R^1=H, R^2=2-CN-Ph, R^3=H) (IC_{50} 6b=27nM, 6c=130nM). Similarly, fluorinated Compound 6g (R^2=F) has lwer activity than the non-fluorinated Compound 6f (R^1=H) (IC_{50} 6f=22nM, 6g=46nM). Compound R^1 R^2 BACE-1 IC_{50} (nM) 6b H 2-CN-Ph 27 6c 3-F 2-CN-Ph 130 6f H 2-CN-3-F-Ph 22 6g 4-F 2-CN-3-F-Ph 46
Exhibit_BMCL_5111 	This publication relates to comparative study for anti-BVDV 및 anti-HCV activity. Table 1 provides anti-BVDV, and anti-HCV activities, wherein Compound 1 has better activity than the fluorinated derivatives, Compounds 2, 3, 5, and 6 in its anti-BVDV activity. In addition, while their anti-HCV activity has mixed result. Compound R^1 R^2 BVDV EC_{50} (mM) HCV EC_{50} (mM) 1 H H 0.12 3.0 2 3-F H 0.24 0.6 3 5-F H 0.50 45 5 6-F H 0.48 75
Exhibit_JMC_7631  11a-e	This reference relates to SAR of HIV-1 inhibitor. Table 3 presents anti-HIV-1 activity and selectivity indexes, wherein the fluorinated compound 11e (R=F) has lower activity than the non-fluorinated Compound 11a (R=H). Compound X R 11a CH H 11e CH F

These results, in addition to the data in the present application support that the substitution of H with F is not an obvious variation of the compounds from the prior art. On page 7-8 of Office Action, the Examiner provides several examples with contradicting conclusions: On page 7, it was indicated that Patani teaches the substitution of H with F should not alter the

biological/pharmaceutical properties but, on page 8 it was indicated that there would be a reasonable expectation of success in this modification.

Examiner's response:

The data presented ion Table 4 further confirms that within certain range, substituting Hydrogen with Fluorine will maintain the biological properties of the parent molecule. Of course, and as discussed above, there is no way to predict the magnitude of the difference in biological behavior, or if it going to be more or less active, but what it is reasonably expected is that if the parent (non-fluorinated molecule) is active, that the Fluorinated counterpart will also be active, more active or less active, but still active within a certain range. In Table 4, Applicant presents examples wherein substituting Hydrogen with Fluorine produces lees activity, but yet the fluorinated compounds are still active.

In summary, all the variations in activity presented by Applicant in Tables 1 through 4, are variations that are expected based on the teachings of the prior art. What would have been "unexpected" is a parent (non-fluorinated) compound for which there is no biological activity known, and then replacing Hydrogen with Fluorine will produce a biologically active molecule. But in the instant case, the parent (non-fluorinated compound A) has already been described as an antitumor agent with significant cytotoxicity against a diverse set of tumor cell lines.

Finally, there was no contradiction in the statements presented in the office action dated 10/20/2010 as inferred by Applicant. On page 7 it was stated that "substituting Hydrogen by Fluorine is routine practice in the pharmaceutical art, and

should no alter the biological/pharmaceutical properties", meaning that the biological/pharmaceutical properties should be similar, in other words one can expect a variation of the magnitude of the biological activity (let's say from -20 to +20) but this does not alter the fact that the activity is still there regardless of the magnitude of the change. So, regardless of the magnitude of the changes, there is a reasonable expectation of success that replacing Hydrogen with Fluorine will result in a molecule with the same or similar biological properties, regardless of the magnitude of the change. So the word "similar", or the phrase "does not alter" refers to the qualitative behavior of these molecules (i.e. if the parent non-fluorinated compound is active against certain biological property it will be expected the corresponding fluorinated compound to have the same property regardless of the magnitude of the activity). Further, and as discussed above, certain magnitudes in the biological behavior are also expected.

Applicant argues that:

The physico-chemical properties may not change much by substitution of H with F. However, the substitution cannot be made a simple one-step substitution reaction in most of the compounds. In the present invention, most fluorinated compounds were not prepared from their non-fluorinated counterpart by fluorine substitution but prepared from a different starting material from several steps in advance. In other words, the compounds having F requires a different synthesis process and thus it would not have

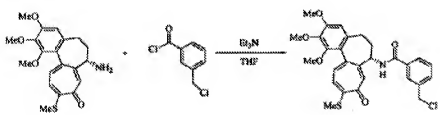
been an easy and obvious choice to those ordinary skilled in the art but would require much endeavor enough to make the choice NON-OBVIOUS.

Examiner's response:

First, Applicant is claiming a compound, and not a synthetic method, so the difficulties in making a compound should not be considered when determining the patentability of a new structure.

Second, the skilled in the art, which is an organic/medicinal chemist, knowing of the existence of compound A which has anticancer properties, will be motivated to make any fluorine substitution in the aromatic ring, because the prior art (i.e. Patani) teaches that, within a reasonable expectation, the fluorinated counterparts will have similar (i.e. worse, equal or better) properties and will have the sufficient knowledge to synthesize the fluorinated compound with a reasonable expectation of success. The difficulties that the skilled in the art might encounter in the synthesis of fluorinated derivatives, will not deter the skilled in the art to further pursue the synthesis of these compounds, since synthesis of new compounds is common practice among organic chemists.

Third, the synthesis of the non fluorinated intermediate (Compound A) is taught by Kim on pages 26 and 28:



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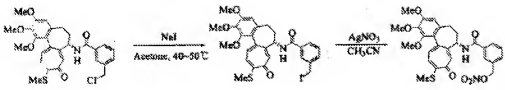

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This synthetic procedure can be adapted, or offer a starting point, to make an aromatic fluorinated compound by simply making a fluorinated benzoyl chloride intermediate and then following the same or similar synthetic steps as taught by Kim (see above).

Applicant argues that:

It was noted that the Examiner indicated that, based on the prior teaching and the other examples in the court, substitution of H with F would not result in any dramatic changes but a equal or some improvement, and thus obvious variation. Applicant respectfully disagrees and would like to reemphasize the result presented in Tables 1 and 2 of this response, wherein the fluorinated compounds made SIGNIFICANT IMPROVEMENT in their biological activity, in contrary to what was known in the art, over the non-fluorinated compound A.

On page 9, claims 18-21 are rejected based on the anti-cancer activity of Compound A of teachings by Kim. Applicant respectfully disagrees. As provided in the above Tables 1-2, the compounds in the instant claims were not merely as effective as

the compounds by Kim but provided SIGNIFICANTLY BETTER ACTIVITY. However, considering other references such as three Exhibits enclosed, other publications teach away from the reasonable expectation of success and thus, it is respectfully urged that the present invention and the instant claims are NOT OBVIOUS over the teachings by the cited references separately or in combination.

Examiner's response

At no point did the Examiner stated: "substitution of H with F would not result in any dramatic changes but a equal or some improvement, and thus obvious variation". As discussed above, this is Applicant's misinterpretation of Examiner's statements that: "substituting Hydrogen by Fluorine is routine practice in the pharmaceutical art, and should no alter the biological/pharmaceutical properties" (see above discussion). And again, as discussed above, what Applicant considers a significant improvement in activity, is just what the skilled in the art would have expected from previous experiences showing that substituting Hydrogen with Fluorine could cause significant improvement in biological activity (see Patani, page 3149, Figure 2, and Table 4).

Double Patenting (Maintained Rejections)

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 12-13 and 16-17 stand rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5 of U.S. Patent No. 7,119,229 in view of Patani et. al. (Chem. Rev. (1996) 96:3147-3176).

Claims 1-5 teach similar compounds and pharmaceutical compositions as claimed in the instant application. The prior art compounds only differ in the absence of an halogen (i.e. F, Cl, Br or I) in the aromatic ring. However, Patani teaches that the substitution of Hydrogen by Fluorine is one of the most commonly employed monovalent isosteric replacements (see page 3149, left column under 1. Fluorine vs. Hydrogen Replacements). Further in Figure 2 on the same page they give an example wherein replacing Hydrogen with Fluorine in an aromatic ring maintains or improves the pharmacological properties of the compounds. In summary, substituting Hydrogen by Fluorine is routine practice in the pharmaceutical art, and should not alter the biological/pharmaceutical properties (see also above 103 rejection).

At the time of the invention, it would have been *prima facie* obvious for a person of ordinary skill in the art to replace any Hydrogen of the aromatic ring of compound A with a Fluorine in order to obtain the instant claimed compounds, and expect these compounds to have the same biological/pharmaceutical properties, since the prior art teaches replacing Hydrogen with Fluorine is routine practice in the pharmaceutical art, in order to obtain molecules with similar or better pharmaceutical properties, thus

resulting in the practice of claims 12-13 and 16-21 with a reasonable expectation of success.

Claims 12-13 and 16-21 stand rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4 of U.S. Patent No. 7,622,612. Although the conflicting claims are not identical, they are not patentably distinct from each other because many, but not all, of the compounds of claims 1-4 of the US Patent are the same as the instantly disclosed compounds.

Response to Applicant's arguments related to the above rejection

This rejection is maintained since applicant has (effectively) not responded to the rejection in a substantive manner. See 37 CFR § 1.111(b) and MPEP § 714.02.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MARCOS SZNAIDMAN whose telephone number is (571)270-3498. The examiner can normally be reached on Monday through Thursday 8 AM to 6 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brandon Fetterolf can be reached on 571 272-2919. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/MARCOS SZNAIDMAN/
Examiner, Art Unit 1628
April 22, 2011.

Withdrawn Rejections and/or Objections

Claims rejected under 35 USC 112, second paragraph .

Applicant's arguments are persuasive; the 112 second rejection is now moot.

Rejection under 35 USC 112, second paragraph is withdrawn.